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Easily Attachable and Detachable *ortho*-Directing Agent for Arylboronic Acids in Ruthenium-Catalyzed Aromatic C−H Silylation

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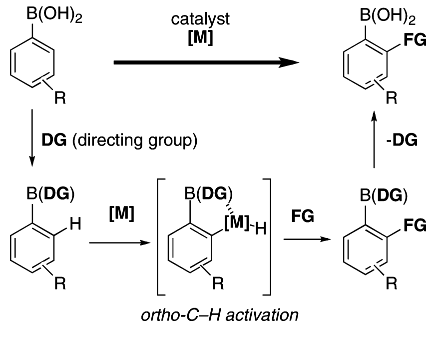
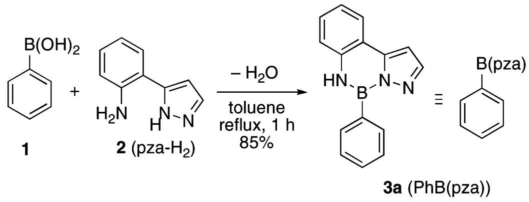
Directed metalation is recognized as an efficient strategy in organic synthesis because of the enhanced reactivity, regioselectivity, and stereoselectivity through coordination of the directing group to a metal.[1] In particular, *ortho*-directed metalation of aromatic compounds has attracted much attention in the synthesis of functionalized arene derivatives.[2] In addition to stoichiometric metalations such as *ortho*-lithiation,[3] recent interest has also focused on *ortho*-C−H activation with transition-metal catalysts.[1c,4] Triggered by the work by Murai and co-workers,[5] *ortho*-directed C−H functionalization of aromatic compounds has become one of the most actively studied areas in organic synthesis. Although one major drawback of the strategy may be limited substrate scope because of the requirement of the *ortho*-directing group itself, a removable directing group has been reported to overcome this limitation.[6] It seems highly attractive to produce new directing groups that are easily attachable to the starting materials and detachable from the products.[7]

In view of the increasing demand for functionalized organoboronic acids in organic synthesis, their efficient synthesis via functionalization of easily available organoboronic acids is highly desirable.[8] It seems quite useful if easily attachable and detachable directing groups can be introduced onto the boron atom of the organoboronic acids (Scheme 1). We herein report the use of 2-pyrazol-5-ylaniline as an easily attachable and detachable *ortho*-directing agent.

Scheme 1. *ortho*-C−H Functionalization of Arylboronic Acids via Temporary Introduction of a Removable Directing Group

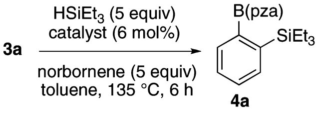


We tested our working hypothesis in ruthenium-catalyzed *ortho*-C−H silylation.[6b,9] In the original reaction system, various oxygen and nitrogen functionalities served as a directing group in the presence of a $Ru_3(CO)_{12}$ catalyst with 3,3-dimethyl-1-butene or norbornene as a hydrogen scavenger. We chose a pyrazole group as an *ortho*-directing element, which could be introduced onto the boron atom via condensation of phenylboronic acid with 2-pyrazol-5-ylaniline (eq 1).[10] The reaction afforded the condensation product **3a** in high yield, which showed reasonable stability toward air and moisture,[11] although it was found to be less stable toward chromatography on silica gel than B(dan) derivatives (dan = naphthalene-1,8-diaminato), which we developed as a protective group for a boronyl group.[12]



(1)

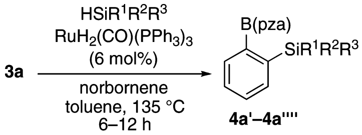
The pza derivative **3a** was subjected to catalytic *o*-silylation with triethylsilane (eq 2). We found that $RuH_2(CO)(PPh_3)_3$ catalyst afforded the corresponding *o*-silylation product in high yield, while $Ru_3(CO)_{12}$ and $[RhCl(cod)]_2$ also afforded the same product in much lower yields. It should be remarked that we did not observe silylation at the other positions. All the control experiments using $PhB(OH)_2$, PhB(pin), and PhB(dan) resulted in no reaction under the same reaction conditions.



catalyst	NMR yield/%
$RuH_2(CO)(PPh_3)_3$	93
$Ru_3(CO)_{12}$	53
$[RhCl(cod)]_2$	16

(2)

The reaction of **3a** with a series of hydrosilanes in the presence of the ruthenium catalyst was examined (eq 3). Phenyl-substituted hydrosilanes afforded the corresponding products **4a′** and **4a″** in high yields. We also obtained $BnMe_2Si$-substituted arene **4a‴**, which can be utilized for further transformation by virtue of the ready cleavage of the Bn−Si bond.[13] Although TBDMS derivative **4a⁗** could be obtained in low yield, the use of bulkier TIPS-H resulted in no reaction. Triethoxysilane gave no desired product under the current reaction conditions.



$HSiR^1R^2R^3$	product	(%yield)
$HSiMe_2Ph$	**4a'**	(98)
$HSiMePh_2$	**4a''**	(91)
$HSiMe_2Bn$	**4a'''**	(88)
$HSiMe_2{}^tBu$	**4a''''**	(35)

(3)

We then carried out the *ortho*-directed silylation of substituted phenylboronic acid derivatives (Table 1). To facilitate the isolation process, the products were converted into the corresponding pinacolate derivatives by treatment of the reaction mixture with pinacol and TsOH.[14] In the series of reactions shown in Table 1, preparation of the (pza)B derivatives (1 equiv **2**) and the subsequent silylation were carried out in one pot without isolating the pza-attached derivatives **3**. This protocol was found to work efficiently, as demonstrated in the reaction of **1a** (entry 1). Arylboronic acids **1b**−**e** bearing *para*-substituents such as methyl, methoxy, trifluoromethyl, chloro, fluoro, and methoxycarbonyl afforded the corresponding *o*-silylated products in moderate to high yields (entries 2−7). Although the product yields showed no remarkable dependence upon the electronic nature of the *para*-substituents, we observed faster reaction for the more electron-rich arene derivatives. Highly regioselective

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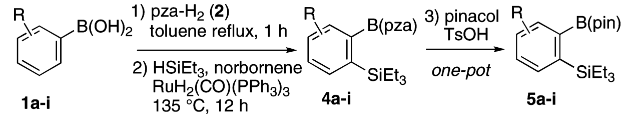
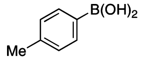
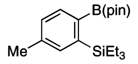
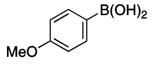
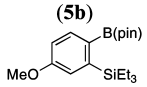
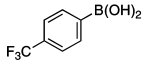
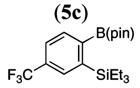
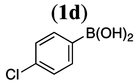
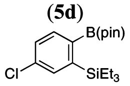
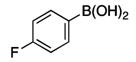
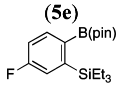
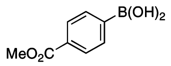
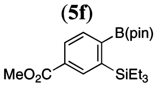
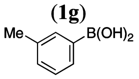
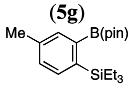
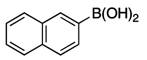
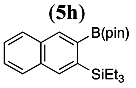
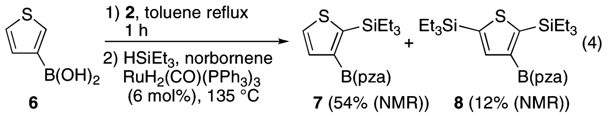
Table 1. One-Pot *o*-Silylation of Arylboronic Acids by Using Pyrazolylaniline as an *ortho*-Directing Agent[a]



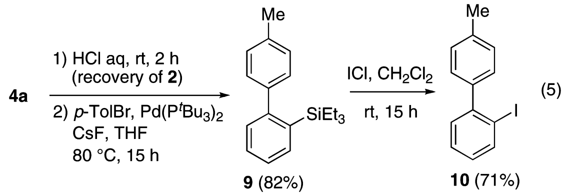
entry	1	% yield[b] 4	% yield[c] 5	isolated product
1	$PhB(OH)_2$ (**1a**)	97 (89)[d,e]	–	**4a**
2	 (**1b**)	94	80	 (**5b**)
3	 (**1c**)	83	77	 (**5c**)
4	 (**1d**)	86	71	 (**5d**)
5	 (**1e**)	85	78	 (**5e**)
6	 (**1f**)	91	84	 (**5f**)
7	 (**1g**)	47	40	 (**5g**)
8	 (**1h**)	88	74	 (**5h**)
9	 (**1i**)	70	62	 (**5i**)

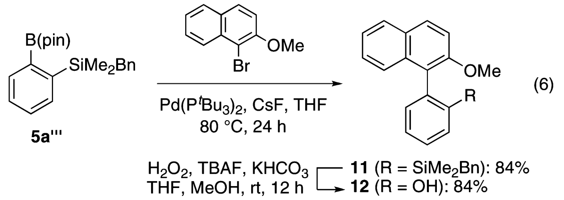
[a] **1a** (0.25 mmol) and **2** (0.25 mmol) were used for the first step. In the second step, $RuH_2(CO)(PPh_3)_3$ (15 μmol), norbornene (1.25 mmol), hydrosilane (1.25 mmol), and toluene (0.13 mL) were used. See Supporting Information for details. [b] NMR yield. [c] Isolated yield. [d] Isolated yield for **4a** in parentheses. [e] $RuH_2(CO)(PPh_3)_3$ (7.5 μmol).

silylation at the less sterically hindered *ortho*-position was observed in the reaction of *m*-tolylboronic acid (**1h**) (entry 8). It should be noted that almost no formation of double silylation products was detected in these reactions. The sluggishness of the second silylation is likely due to steric factors, since no *o*-silylation was observed at all with *o*-tolylboronic acid.[15] 2-Naphthylboronic acid (**1i**) underwent silylation at the 3-position (entry 9). 3-Thiopheneboronic acid **6** also underwent the directed silylation selectively at its 2-position, although applying a longer reaction time resulted in further silylation at the 5-position, which was not assisted by the directing group (eq 4).[16]



The silylated areneboronic acids served as convenient building blocks for the synthesis of functionalized biaryl derivatives through Suzuki−Miyaura coupling.[17] Silylated product **4a** was transformed into the corresponding boronic acid by an acid treatment and subjected to Suzuki−Miyaura coupling with *p*-tolyl bromide (eq 5). In this reaction, pza-H_2 (**2**) was recovered in 85% yield on acid treatment. The silyl group of **9** was substituted with iodine by treatment with ICl to give biaryl iodide **10**. In another transformation, the silyl group of cross-coupling product **11** was converted into a hydroxy group by Tamao−Fleming oxidation,[12,18] leading to the formation of naphthyl-substituted phenol **12** (eq 6).





In summary, we have reported a new protocol for *ortho*-C-H functionalization of arylboronic acids by using 2-pyrazol-5-ylaniline as an *ortho*-directing group. The key feature of the new directing group is the ease of its installation and removal. Generalization of this protocol to other *o*-C-H functionalizations is now being undertaken in this laboratory.

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Supporting Information Available: Experimental procedures and spectral data for the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) 2-Pyrazol-5-ylaniline was prepared via three steps from *o*-nitroacetophenone in 83% overall yield. See the Supporting Information.
(11) PhB(pza) showed no decomposition over at least 10 months on storage in a vial in air.
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(14) Some of the produced B(pin) derivatives were still unstable toward silica gel column chromatography.
(15) Silylation of the benzylic C−H bond proceeded slowly in low yield.
(16) Nondirected, Ir-catalyzed silylation of thiophenes has been reported: Lu, B.; Falck, J. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 7508.
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